

That which is claimed is:

1. A method for modulating the expression of an exogenous gene in a mammalian subject containing:

- (i) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a silent partner therefor, binds to a response element, and wherein said modified ecdysone receptor comprises: (a) a ligand binding domain that binds to an ecdysteroid, (b) a DNA-binding domain obtained from a DNA-binding protein, which binds to said response element; and (c) an activation domain of a transcription factor, wherein at least one of said DNA-binding domain or said activation domain is not obtained from a native ecdysone receptor, with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an *E. coli* LexA protein; and
- (ii) a DNA construct comprising said exogenous gene under the control of said response element, wherein said response element (a) has about 12-20 base pairs, (b) binds to said modified ecdysone receptor, and (c) does not bind to farnesoid X receptor (FXR);

said method comprising providing to said subject an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in said subject; and wherein said one or more ligands are not toxic to said subject.

2. A method of inducing the expression of an exogenous gene in a mammalian subject containing:

- (i) DNA encoding a modified ecdysone receptor under the control of an inducible promoter, wherein said modified ecdysone receptor, in the presence of a ligand therefor, and optionally in the further presence of a silent partner therefor, binds to a response element, and wherein said modified ecdysone receptor comprises: (a) a ligand binding domain that binds to an ecdysteroid, (b) a DNA-binding domain obtained from a DNA-binding protein, which binds to said

response element; and (c) an activation domain of a transcription factor, wherein at least one of said DNA-binding domain or said activation domain is not obtained from a native ecdysone receptor, with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein;

(ii) a DNA construct comprising said exogenous gene under the control of said response element, wherein said response element (a) has about 12-20 base pairs, (b) binds to said modified ecdysone receptor, and (c) does not bind to farnesoid X receptor (FXR); and

(iii) one or more ligands for said modified ecdysone receptor;

said method comprising subjecting said subject to conditions suitable to induce expression of said modified ecdysone receptor.

3. A method of inducing expression of an exogenous gene in a mammalian subject containing a DNA construct containing said exogenous gene under the control of a response element, wherein said response element (a) has about 12-20 base pairs, (b) binds to a modified ecdysone receptor, and (c) does not bind to farnesoid X receptor (FXR), said method comprising introducing into said subject:

a modified ecdysone receptor, wherein said modified ecdysone receptor comprises: (a) a ligand binding domain that binds to an ecdysteroid, (b) a DNA-binding domain obtained from a DNA-binding protein, which binds to said response element; and (c) an activation domain of a transcription factor, wherein at least one of said DNA-binding domain or said activation domain is not obtained from a native ecdysone receptor, with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein; and

one or more ligands for said modified ecdysone receptor,

wherein said modified ecdysone receptor, in combination with a ligand therefor, and optionally in the further presence of a silent partner therefor, binds to said response element, activating transcription therefrom.

4. A method for modulating the expression of an exogenous gene in a mammalian subject containing:

- (i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element; and
- (ii) a modified receptor which, in the presence of a ligand therefor, and optionally in the further presence of a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor does not bind to endogenous response elements, and wherein said modified receptor comprises: (a) a ligand binding domain that binds to an ecdysteroid; (b) a DNA-binding domain derived from a DNA-binding protein, wherein said DNA-binding domain binds to said ecdysone response element but not to endogenous response elements; and (c) an activation domain of a transcription factor, with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an *E. coli* LexA protein;

said method comprising providing to said subject an effective amount of one or more ligands for said modified receptor; wherein said one or more ligands are not normally present in said subject; and wherein said one or more ligands are not toxic to said subject.

5. A method of inducing the expression of an exogenous gene in a mammalian subject containing:

- (i) a DNA construct comprising an exogenous gene under the control of an ecdysone response element,
- (ii) DNA encoding a modified receptor under the control of an inducible promoter, wherein said modified receptor, in the presence of a ligand therefor, and optionally in the further presence of a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor does not bind to endogenous response elements, and wherein said modified receptor comprises: (a) a ligand binding domain that binds to an ecdysteroid; (b) a DNA-binding domain derived from a DNA-binding protein, wherein said DNA-binding domain binds to said ecdysone response element but not to endogenous response elements; and (c)

an activation domain of a transcription factor, with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein;

(iii) one or more ligands for said modified receptor;

said method comprising subjecting said subject to conditions suitable to induce expression of said modified receptor.

6. A method of inducing expression of an exogenous gene in a mammalian subject containing a DNA construct containing said exogenous gene under the control of an ecdysone response element, said method comprising introducing into said subject:

a modified receptor, wherein said modified receptor does not bind to endogenous response elements, and wherein said modified receptor comprises: (a) a ligand binding domain that binds to an ecdysteroid; (b) a DNA-binding domain derived from a DNA-binding protein, wherein said DNA-binding domain binds to said ecdysone response element but not to endogenous response elements; and (c) an activation domain of a transcription factor, with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein; and

one or more ligands for said modified receptor,

wherein said modified receptor, in the presence of a ligand therefor, and optionally in the further presence of a silent partner therefor, binds to said ecdysone response element, activating transcription therefrom.